REMARKS

Reconsideration and allowance are respectfully requested.

Claims 6-15 and 20-30 are pending. The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. Support for the claim amendment may be found, inter alia, at page 11, lines 11-12, of the specification.

35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See id. ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See id. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a prima facie case under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. An inquiry is required as to "whether the improvement is more than the predictable use of prior art elements according to their established functions." Id. at 1396. But a claim that is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Id. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 6, 8-11, 13 and 20-29 were rejected under Section 103(a) as allegedly unpatentable over Tanekawa et al. (U.S. Patent 4,303,680) in view of Keller et al. (U.S.

Patent 4,623,723) with evidence provided by Kanegae et al. (U.S. Patent 4,810,509) and Chae et al. (Bioresource Technol. 76:253-258, 2001). Applicants traverse.

The Examiner alleged that it would have been obvious to one of ordinary skill in the art at the time this invention was made to improve the process for producing a flavoring composition containing 5'-ribonucleotides disclosed by Tanekawa with Keller's method of separating RNA from other soluble cell material. Applicants disagree.

The present claims require separation of RNA (i.e., a high molecular weight material) from low molecular weight soluble cell materials. Independent claims 6 and 20 specify that "the other soluble cell material" (i) is smaller than 50 kDa and (ii) comprises peptides and small proteins. See Example 2, especially page 11, lines 9-12, of Applicants' specification. Claims 8-11, 13 and 21-29 depend from these independent claims and, thus, they contain the same limitations.

By contrast, Keller uses filtration to separate RNA from DNA (both high molecular weight materials), instead of separating RNA from low molecular weight soluble cell materials that (i) are smaller than 50 kDa and (ii) comprise peptides and small proteins as required by Applicants' claims. One of ordinary skill in the art would know that DNA is much larger than 50 kDa, and hence that the low molecular weight material as defined in Applicants' specification cannot possibly be DNA.

Keller neither explicitly nor implicitly separates RNA from other soluble cell material smaller than 50 kDa comprising peptides and small proteins because it was well known in the art that proteins precipitate at pH 2.0. Applying an acidification step (pH 2.0) is not a suitable way to separate RNA from other soluble cell material smaller than 50 kDa comprising peptides and small proteins because the would all precipitate.

The reason that Keller uses an acidification (pH 2.0) step to isolate the RNA from the nucleic acid solution is probably that - in both Examples - there is no other soluble cell material smaller than 50 kDa comprising proteins in the solution:

- Example 1 of Keller added methanol/ammonia to the heat-treated cells (column 2, lines 19-22) followed by a solid/liquid separation, whereby the nucleic acid is in the liquid fraction (see column 2, lines 27-33). One of ordinary skill in the art would have

known that adding methanol results in precipitation of proteins. Thus, the nucleic acid in the supernatant of Example 1 has been separated from proteins.

- Example 2 of Keller used a crude nucleic acid solution obtained according to Example 8 of U.S. Patent 4,206,243, from which the protein has also been separated (column 5, lines 51-53, of the '243 patent).

Thus, in both Examples, the nucleic acid solution to which Keller applies an acidification (pH 2.0) step is free of proteins. In contrast, according to Applicants' claimed process, the released cell contents contain not only RNA but also other soluble cell material smaller than 50 kDa comprising peptides and small proteins, which material would precipitate at pH 2.0.

In accordance with Applicants' claimed invention, it is highly likely that RNA and DNA would both be retained in the same fraction if filtration was used for separation. Therefore, one of ordinary skill in the art seeking to modify Tanekawa's process so that RNA is separated from low molecular weight soluble cell material would not have combined it with Keller because the latter teaches the separation of RNA from DNA.

Finally, no reasonable expectation of success was provided by the Examiner to combine Tanekawa and Keller to separate RNA from low molecular weight soluble cell materials that (i) are smaller than 50 kDa and (ii) comprise peptides and small proteins.

For the foregoing reasons, the combination of Tanekawa and Keller does not render obvious Applicants' invention as represented by independent claims 6 and 20. Moreover, dependent claims 8-11, 13 and 21-29 are also not rendered obvious by the cited documents because all limitations of an independent claim are incorporated in its dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore, this obviousness rejection should be withdrawn.

Claims 12 and 30 were rejected under Section 103(a) as allegedly unpatentable over Tanekawa in view of Keller, further in view of Fernandez et al. (Acta Biotechnol. 12:49-56, 1992). Applicants traverse.

Tanekawa and Keller were previously discussed. For reasons explained above regarding the Examiner's allegation that independent claim 6 is rendered obvious by Tanekawa in view of Keller, the two documents' failure to disclose the claimed invention

is not remedied by the attempt to combine their disclosures with Fernandez. The latter document was only cited for using ultrafiltration for concentrating and/or fractionating RNA from an ammonia yeast extract instead of separating RNA from soluble cell materials (i) smaller than 50 kDa and (ii) comprising peptides and small proteins as required by Applicants' claims. In accordance with Fernandez's protocol, a cell suspension is alkalinized with ammonium water and then extracted to yield an RNA-containing supernatant (see paragraph bridging pages 49-50).

Among those failures is the lack of a reasonable expectation of success that the prior art process would separate RNA from low molecular weight soluble cell material like peptides and small proteins. There is nothing either explicit or implicit in the record that this extract contains the soluble cell materials required by Applicants' claims. In fact, since it appears likely that the macrosolutes of Fernandez are nucleic acids (see page 49), there is nothing to teach or suggest that peptides and small proteins are separated from RNA during Fernandez's ultrafiltration. Applicants submit that this feature of their claimed invention is sufficient to distinguish over the cited documents so any other incorrect allegations about their disclosures are not disputed here, but the opportunity to dispute them in the future is reserved.

Thus, the combination of Tanekawa, Keller, and Fernandez does not render obvious Applicants' invention as represented by independent claim 6 and 30. Moreover, dependent claim 12 is also not rendered obvious by the cited documents because all limitations of an independent claim are incorporated in its dependent claim. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore, this obviousness rejection should be withdrawn.

Claims 6-7 and 25 were rejected under Section 103(a) as allegedly unpatentable over Tanekawa in view of Keller, further in view of Potman et al. (U.S. Patent 5,288,509). Applicants traverse.

Tanekawa and Keller were previously discussed. For reasons explained above regarding the Examiner's allegation that independent claim 6 is rendered obvious by Tanekawa in view of Keller, the two documents' failure to disclose the claimed invention is not remedied by the attempt to combine their disclosures with Potman. The latter

document was only cited for an earlier processing step of treating cells with a protease, which is before the initial separation of RNA from DNA, to deactivate native enzymes prior to the cell's enzymatic degradation, instead of the later step of separating RNA from soluble cell materials (i) smaller than 50 kDa and (ii) comprising peptides and small proteins as required by Applicants' claims.

Among those failures is the lack of a reasonable expectation of success that the prior art process would separate RNA from low molecular weight soluble cell material like peptides and small proteins. Applicants submit that this feature of their claimed invention is sufficient to distinguish over the cited documents so any other incorrect allegations about their disclosures are not disputed here, but the opportunity to dispute them in the future is reserved.

Thus, the combination of Tanekawa, Keller, and Potman does not render obvious Applicants' invention as represented by independent claim 6. Moreover, dependent claims 7 and 25 are also not rendered obvious by the cited documents because all limitations of an independent claim are incorporated in its dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore, this obviousness rejection should be withdrawn.

Claims 6 and 14-15 were rejected under Section 103(a) as allegedly unpatentable over Tanekawa in view of Keller, further in view of Tsuda et al. (U.S. Patent 4,374,981). Applicants traverse.

Tanekawa and Keller were previously discussed. For reasons explained above regarding the Examiner's allegation that independent claim 6 is rendered obvious by Tanekawa in view of Keller, the two documents' failure to disclose the claimed invention is not remedied by the attempt to combine their disclosures with Tsuda. The latter document was only cited for a later processing step of separation, which is after the initial separation of RNA from DNA, to further purify the 5'-ribonucleotides by the removal of compounds having a higher molecular weight than 5'-ribonucleotides, instead of the earlier step of separating RNA from soluble cell materials (i) smaller than 50 kDa and (ii) comprising peptides and small proteins as required by Applicants' claims.

Among those failures is the lack of a reasonable expectation of success that the prior art process would separate RNA from low molecular weight soluble cell material like peptides and small proteins. Applicants submit that this feature of their claimed invention is sufficient to distinguish over the cited documents so any other incorrect allegations about their disclosures are not disputed here, but the opportunity to dispute them in the future is reserved.

Thus, the combination of Tanekawa, Keller, and Tsuda does not render obvious Applicants' invention as represented by independent claim 6. Moreover, dependent claims 14-15 are also not rendered obvious by the cited documents because all limitations of an independent claim are incorporated in its dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore, this obviousness rejection should be withdrawn.

Withdrawal of the Section 103 rejections is requested because the claims would not have been obvious to one of ordinary skill in the art when this invention was made.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

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